WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

AT WASHINGTON UNIVERSITY MEDICAL CENTER

DEPARTMENT OF GENETICS

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Dr. Joshua Lederberg
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I assume you are running chemostats under carbon (galactose) limitation. This will stress just one aspect of permease/lactase function — a facility for very low concentration

Dear Josh:

It is good to know you still have time to read in evolutionary biology in spite of your heavy administrative duties.

Enclosed is the paper with Tony Dean you requested. The experimental material consists of amino acid replacements in the lacZ β-galactosidase obtained as spontaneous revertants of nonsense codons that restored enzyme synthesis but altered its electrophoretic mobility or thermostability as compared with wildtype. The result was unexpected in that most of the amino acid replacements produced effects too small to be detected in chemostat competition experiments with the parental wildtype strain. Among 25 amino acid replacements in β-galactosidase obtained in 17 codons distributed approximately uniformly along the gene, only three produced selective effects large enough to be significant in chemostats. The remaining 22 produced effects that could not be detected under conditions in which the limit of resolution was a selection coefficient of approximately 0.4 percent per generation. I suspect that many of the amino acid replacements actually resulted in small differences in enzyme activity, but that these gave undetectable effects in chemostats owing to the small control coefficient of β-galactosidase with respect to fitness.

Doesn't prevent selection (drift) interfere with presumed merit of selective advantage

Best regards for the holiday season and best wishes for a healthy and happy New Year.

Thank you, Dan.
My interest in this title has to do with the "cost of evolution", harking back to a paper by Kimura many years ago. It is now known that there are far less than $\approx 6 \times 10^9$ bits of information in the human genome — which has some bearing on cost-effective strategies for understanding it.

Sincerely,

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Yours, J.L.